REMARKS

Support for the above amendments to claim 1 is provided in the specification and claims as originally filed. As the Examiner will no doubt note, much of the amendments simply reiterates subject matter that was present in the claim as originally filed. In addition to support from the claim as originally filed, the Examiner's attention is respectfully directed to at least page 6, lines 27-32.

Similarly, claim 3 has been amended to re-iterate subject matter that was present in the claim as originally filed.

Claims 7, 9 and 10 have been amended to correct typographical and grammatical errors. The claims have also been amended with respect to language present in claim 1 and to re-phrase the language of subject matter that was present in the claims as originally filed.

None of these amendments have altered the scope of the claims from that which was originally intended. The amendments have been made for reasons related to business considerations and not in acquiescence to any reason related to patentability.

New claims 13-18 correspond to pending claims 5-10 (as amended) except that new claims 13-18 are dependent from independent claim 3. No new matter has been introduced and entry of the above amendments is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the above amendment. The attached pages begin with the caption **"Version with markings to show changes made."**

Restriction Requirement

The Office Action mailed November 6, 2001 refers to Applicants' election on August 16, 2001 of Group I (claims 1, 3 and 5-10) as having been made with traverse.

Applicants wish to respectfully point out that this appears to be in error because the election of Group I was made without traverse.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 3 and 5-10 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants have carefully reviewed the statement of this rejection and traverse as follows.

Part "A" of the statement asserts that the term "specific and binding and comprising" as used in claim 1 are "relative terms, which render the claim indefinite". The statement also asserts that the term "specific binding derivatives or fragments" is not defined by the claims, that the specification also does not define the term, and that a skilled artisan would not be aware of the scope of the term.

As an initial matter, Applicants are unable to locate either of the quoted terms in independent claim 1 or 3 as originally filed or as amended. Neither "specific and binding" or "derivatives or fragments" are used anywhere in claim 1 or 3. Additionally, Applicants are confused as to how the transitional term "comprising" can be indefinite in light of clear interpretations under U.S. law as to its meaning.

To the extent that claims 1 and 3 previously recited the term "specific binding" with respect to peptide(s) as recited in the claims, Applicants respectfully point out that the term has been amended to "binding" which is a concept readily understood by the skilled artisan with respect to a peptide and a proteinaceous target to which the peptide binds.

Applicants respectfully submit that the assertion of indefiniteness in part "A" of the rejection may be properly withdrawn.

Part "B" of the rejection asserts that claim 3 provides "no metes and bounds regarding which peptides capable of binding and peptides not capable of binding , nor the relative information of synthesizing oligopeptides derived from the proteinaceous target...."

Applicants respectfully submit that this rejection appears to be based on a misapprehension of the claimed invention as encompassed by claim 3. Claim 3, as originally filed and as amended, is directed to a method of *distinguishing* peptides that bind oligopeptides (synthesized on a solid phase) derived from a proteinaceous antigen from peptides that do not bind by washing away display packages with non-binding peptides on their surface. As such, and while Applicants do not understand why the claim should provide the "metes and bounds" as to which peptides bind and which do not, the ability to bind oligopeptides on a solid phase (so as to not be "washed away") is what distinguishes peptides that bind from peptides that do not bind.

Moreover, the instant application provides evidence that no information concerning the specific structure of the binding peptide is necessary to identify a peptide that binds a particular oligonucleotide. Pages 15-18 and Figure 2 demonstrate how a synthetic phage antibody display library can be produced and used to identify a scFv clone that binds a particular CD64 oligopeptide.

Moreover, and with respect to "relative information of synthesizing oligopeptides derived from the proteinaceous target", Applicants respectfully submit that knowledge concerning the preparation of oligopeptides based on the amino acid sequence of a protein is well understood in the art and that no issue of indefiniteness is present with respect to the concept as present in claim 3.

Part "C" asserts that claim 7 is indefinite with respect to the term "encoding sequence". While Applicants believe that the term taken in the context of "peptide is displayed ... by insertion of its encoding sequence in a gene" is not indefinite in claim 7 as originally filed, claim 7 has been amended to use other language to refer to the identical concept without altering the scope of the claim. Applicants respectfully submit that no issue of indefiniteness is present in the previous version of the claim or in the current version of the claim.

Part "D" asserts that claim 9 is indefinite for use of the term "preferably". The claim has been amended to remove the use of the term.

In light of the above discussion, Applicants respectfully submit that no issue of indefiniteness is present in any of the claims, and that the rejection may be properly withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 3 and 5-10 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention an a manner commensurate with the scope of the claims. Applicants

have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of lack of enablement has been presented.

The rejection asserts that the claims are only enabled for methods using "proteinaceous targets as described in specification page 1". Applicants respectfully submit that this rejection is not understood because page 1 of the specification only discusses the use of binding peptides, such as antibodies and peptides thereof, which may be expressed on the surface of a replicable genetic package and used to bind to a target molecule. The page does not include a discussion of the nature of the target molecule. As such, Applicants are confused as to what subject matter the Examiner considers enabled.

Applicants have also reviewed the remainder of the statement of the rejection and remain confused as to the focus of the rejection. Applicants believe that the following brief summary of the invention will be useful for comparison with the remainder of the statement of the rejection.

The methods of the claimed invention essentially involve the acts of

> displaying peptide(s), that are capable of binding a proteinaceous target (claim 1) or antigen (claim 3) on the surface of replicable display package(s);
>
> synthesizing, on a solid phase, oligopeptides derived from a proteinaceous target; and
>
> contacting the display package(s) with the oligopeptides on the solid phase.

Claim 1 is directed to the use of these acts to identify peptide(s) that bind to the oligopeptides while claim 3 is directed to the use of these acts to distinguish between peptides that bind from those that do not bind (and would thus be "washed away" as recited in the claim).

With respect to "breadth of the claims", page 4 of the Office Action asserts that the breadth of the claims is "huge" and that there is a "failure to specifically claim the metes and bounds regarding the chemical nature of the peptide and the fixated chemical target portions" because "indefinite" terms are used in the claims. But as discussed above with regard to the rejection for indefiniteness, the claims have been amended to address the Examiner's concerns with regard to specific terms used in the claims.

Additionally, Applicants respectfully point out that as set forth at MPEP 2173.04 a broad term is not necessarily indefinite. For example, the term "infinity", while broad, is nevertheless understood by a skilled person without unnecessary confusion or ambiguity. Similarly, a skilled person would recognize that the term "peptide capable of binding" a proteinaceous target or antigen refers to a "peptide" (a term recognized in the art as referring to a particular arrangement of amino acids by use of peptide bonds) that possess a particular functional characteristic of binding. A skilled person would also recognize that "peptides on the surface of a replicable display package" refers to "peptides" that are expressed on the surface of genetic display packages as described on page 4, line 31, to page 5, line 14. The skilled person would also recognize that oligopeptides derived from a "proteinaceous target" or a "proteinaceous antigen" refer to peptides that are prepared based on the amino acid sequence of a "proteinaceous" molecule.

While each of the above terms and concepts are broad, they are certainly not indefinite, and as the Examiner will no doubt appreciate, the breadth of a claim does not necessarily indicate that undue experimentation is required to practice the claimed invention.

Moreover, and as explained above, pages 15-18 and Figure 2 of the specification demonstrate how no specific structure information concerning a binding peptide (on a scFv clone) is necessary to identify it as binding a particular CD64 oligopeptide.

With respect to "nature of the invention/state of the prior art", page 5 of the Office Action asserts that the claimed invention is "broadly directed to any method of identifying a peptide" comprising display of the peptide on a display package and synthesizing oligopeptides. Applicants respectfully, and strongly, disagree. As noted above, claim 1 is directed to the use of binding interactions between a displayed peptide and oligopeptides on a solid phase to identify peptides that bind said oligopeptides. Claim 3 is directed to the use of the same binding interactions to distinguish peptides that bind from those that do not.

The claims are thus directed to methods comprising specific actions which render the claims patentable. Additionally, and contrary to the top of page 5 of the Office Action, that the instant specification provides ample guidance in addition to knowledge in the art concerning the synthesis of oligopeptides on a solid phase (see for example page 7, lines 20-24, and page 15, line 29 to page 17, line 11). As such, Applicants respectfully submit that no "critical or essential

parameters to practice the invention" are lacking from the claims or the specification, and that the assertion of *In re Mayhew* and *Ex parte Bhide* is misplaced.[1]

With respect to "the amount of direction/working examples", page 5 of the Office Action asserts that insufficient guidance is provided as to the specific peptide(s) that would bind a proteinaceous target or antigen. The apparent requirement for such guidance again appears to be based on a misapprehension of the invention. As discussed above, the invention is directed to *identifying* peptides that bind and not merely confirming binding by peptides that are already known to bind.[2] As such, there can be no reason why a skilled artisan would require such guidance to practice the invention. A skilled artisan can certainly conduct the actions of the claimed invention as discussed above without undue experimentation.

With respect to "quantity of experimentation", page 5 of the Office Action asserts that there is a "lack of representative examples regarding the method of identification, and binding specificity of a representative sample of peptide the amount of experimentation would be undue." This assertion is contrary to the working examples provided in the specification as well as the standard for determining undue experimentation only after reviewing the non-exclusive list of factors as set forth in *In re Wands* as noted in the Office Action.

Nowhere in the instant rejection, however, is there a determination of a level of unpredictability which, when combined with a review of the other factors, results in the conclusion that undue experimentation is needed to practice the invention as claimed. As the Examiner is no doubt aware, the standard for enablement is whether ***undue*** (or otherwise *de novo*) experimentation would be required to make and use the invention as claimed (see MPEP 2164.01). As long as a skilled artisan can make and use (or otherwise practice) the acts of the claimed methods in a ***routine*** manner (and thus with routine experimentation), the claims must be viewed as objectively enabled. There has been no objective evidence presented as to why the acts of the claimed methods would require anything other than routine display of peptides, synthesis of oligopeptides on a solid phase, and contacting the displayed peptides with the oligopeptides on the solid phase.

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[1] Especially because *Bhide* primarily concerns issues of utility as opposed to enablement.

[2] Although the invention may of course be used to confirm binding by a peptide known to bind or be suspected of binding.

In the absence of anything except routine experimentation, the invention cannot, as a matter of law, be held as requiring undue experimentation for its practice. For this reason and the discussion provided above, no *prima facie* case of lack of enablement has been presented, and Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 1, 5-7 and 10 are rejected under 35 U.S.C. § 102(b) as allegedly being clearly anticipated by Ladner et al. (WO 92/15677). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of anticipation has been presented.

A review of the reference shows that it is directed to the display of peptides on the surface of a genetic package (see pages 45-70) and use thereof to identify peptides that bind a target of interest (see pages 72-74).

The reference completely fails, however, to disclose the synthesis of oligopeptides, on a solid phase, derived from a proteinaceous target. This deficiency is a failure to disclose a recited element of the invention as encompassed by claims 1, 5-7 and 10.

MPEP 2131 and the cases cited therein reiterate the well settled standard that anticipation requires that a reference teach every element of a claim. In light of the above identified deficiency in Ladner et al., Applicants respectfully submit that no *prima facie* case of anticipation has been presented and request that this rejection be withdrawn.

Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as allegedly being clearly anticipated by Mehta et al. (WO 92/08738) in light of Ishikawa . Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of anticipation has been presented.

A review of Mehta et al. shows that they describe the contacting of a sample with antibodies or fragments thereof immobilized on a solid phase and detecting binding of material to the solid phase (see for example page 3, lines 23-33).

The reference completely fails, however, to disclose the use of a display package or the synthesis of oligopeptides, on a solid phase, derived from a proteinaceous target.

Ishikawa fails to rectify these deficiencies.

These references thus fail to disclose recited elements of the invention as encompassed by claims 1 and 3.

As noted above, no anticipation is possible if a reference does not teach every element of a claim. In light of the above identified deficiencies, Applicants respectfully submit that no *prima facie* case of anticipation has been presented and request that this rejection be withdrawn.

Claims 1, 3 and 5-10 are rejected under 35 U.S.C. § 102(b) as allegedly being clearly anticipated by Catherine et al. (USP 5,844,093). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of anticipation has been presented.

As an initial matter, Applicants believe that the cited reference has been mis-identified. The inventors of USP 5,844,093 include an A. Cathrine Kettleborough but no one with "Catherine" as a last name. Applicants believe, however, that the indication of USP 5,844,093 is correct and have thus responded on this basis. Applicants respectfully request clarification of the rejection should this belief be incorrect.

A review of the reference shows that it is directed to the identification of new anti-EGFR antibodies and scFvs thereof from display libraries that are contacted with purified EGFR (see for example column 4, lines 1-19).

The reference completely fails, however, to disclose the synthesis of oligopeptides, on a solid phase, derived from a proteinaceous target. The reference actually does not even use the terms "oligopeptide" or "solid phase". These deficiencies reflect a failure to disclose recited elements of the invention as encompassed by claims 1, 3 and 5-10.

As noted above, no anticipation is possible if a reference does not teach every element of a claim. In light of the above identified deficiencies, Applicants respectfully submit that no *prima facie* case of anticipation has been presented and request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1 and 3 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Barsomian et al. (WO 95/15982). Applicants have carefully reviewed the statement of the rejection and respectfully submit that no *prima facie* case of obviousness has been presented.

As noted in the statement of the rejection, Barsomian et al. disclose use of display libraries to identify antibodies and fragments thereof that bind an immunosuppressive epitope (see for example page 2, line 26, to page 3, line 3).

Contrary to the statement of the rejection, however, the reference differs from the claimed invention at least in that Barsomian et al. completely fail to disclose the synthesis of oligopeptides, on a solid phase, derived from a proteinaceous target and the use thereof to contact peptides displayed on a replicable display package.

Because no suggestion or motivation has been provided as to why it would have been obvious at the time of the invention for one of ordinary skill in the art to modify Barsomian et al. to include the synthesis of oligopeptides, on a solid phase, derived from a proteinaceous target and the use thereof to contact peptides displayed on a replicable display package, no *prima facie* case of obviousness has been presented. See MPEP 2143, 2143.01, and 2143.03.

Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants believe that the claims are in condition for allowance and urge passage of the application to issue. The Examiner is invited to contact Applicants' agent at the number listed below if it would be helpful in any way to resolve any remaining issues.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 313632000600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated:March 1, 2002

By: _____

Kawai Lau, Ph.D.
Registration No. 44,461

Morrison & Foerster LLP
3811 Valley Centre Drive,
Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5178
Facsimile: (858) 720-5125

Version with markings to show changes made.

1.(amended) A method for identifying a peptide capable of [specific] binding to a proteinaceous target[,] comprising

displaying the peptide on the surface of a replicable display package,

synthesizing oligopeptides derived from the proteinaceous target on a solid phase, [and]

contacting the [specific] binding peptide on the surface of said package with the [oligopeptide to allow for binding] oligopeptides on said solid phase, and

identifying whether binding occurs.

3. (amended) A method for distinguishing between peptides capable of [specific] binding to a proteinaceous antigen and peptides not having that capability comprising

displaying candidate peptides on the surfaces of [a] replicable display packages,

synthesizing oligopeptides derived from the proteinaceous antigen on a solid phase, [and]

contacting the candidate peptides on the surfaces of said packages with the oligopeptides [to allow for binding] on said solid phase to permit binding by said candidate peptides, and

washing the solid phase to remove [the] unbound display packages[not specifically bound].

7. (amended) A method according to claim 5, whereby the [specific] binding peptide is [diplayed] displayed on the surface of the phage particle by insertion of [its encoding sequence] a genetic sequence encoding said peptide in a gene encoding a surface protein of said phage particle.

9. (amended) A method according to claim 1 whereby the [specific binding] displayed peptide is a single chain antibody fragment[, preferably] or an ScFv.

10. (amended) A method according to claim 1, further comprising a step whereby the displayed peptide[s are] is contacted with a sample not containing [the target of interest] said oligopeptides.